## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

SCHWEIGHOFFER et al. Atty. Ref.: 3665-167; Confirmation No. 5165

Appl. No. 10/560,774 TC/A.U. 1617

Filed: December 14, 2005 Examiner: Javanmard

For: USE OF PYRAZOLOPYRIDINES FOR THE TREATMENT OF COGNITIVE

**DEFICITS** 

\* \* \* \* \* \* \* \* \* \* \* \*

May 11, 2009

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

## REQUEST FOR RETURN OF INITIALED COPY OF PTO 1449 FORM FILED JANUARY 23, 2009

Return of an initialed copy of the PTO 1449 Forms filed January 23, 2009 is requested.

The Examiner states in the Office Action dated April 20, 2009 that the documents cited in the PTO 1449 Form were not available to the Examiner at the time of the mailing of the Office Action.

The applicants submit, with due respect to the Examiner, that the references noted below were contained in the PTO IFW as of January 23, 2009. Consideration of the following in this regard is requited.

A copy of the following listed documents is not contained in the PTO IFW and were not filed January 23, 2009: Brighina et al, "Recent Advances in the Therapy of

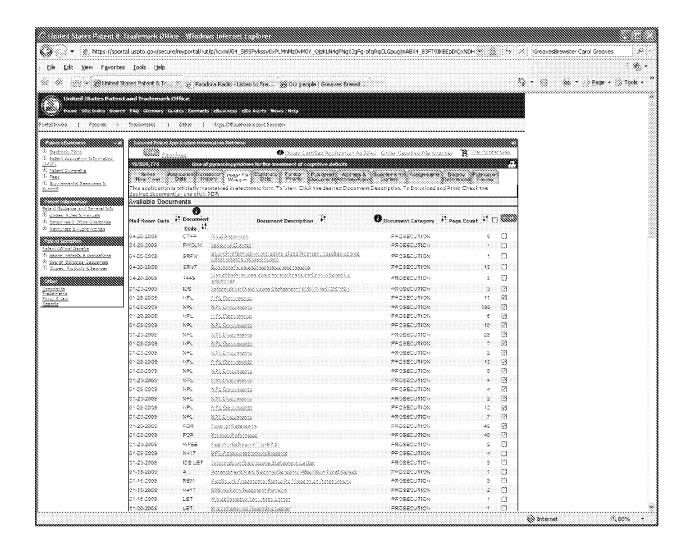
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Amyotrophic Lateral Sclerosis: Focus on Excitotoxicity", FUNCTIONAL NEUROLOGY (16), Suppl. 4, 2001, pp. 189-292; and Rowland et al, "Amyotrophic Lateral Sclerosis", N. ENGL. J. MED., Vol, 344, No. 22, May 31, 2001, pp. 1688-1700. The undersigned has requested a copy of these documents and will file same once received by the undersigned.

The following is a screen shot of the PTO IFW on May 10, 2009:



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**JANUARY 23, 2009** 

The above screen shot of the IFW demonstrates that the following documents were contained in the IFW when the Office Action of April 20, 2009 was mailed:

- 1. 01-23-2009 NPL Documents PROSECUTION (11 pages)
- 2. 01-23-2009 NPL NPL Documents PROSECUTION (180 pages)
- 3. 01-23-2009 NPL NPL Documents PROSECUTION (6 pages)
- 4. 01-23-2009 NPL NPL Documents PROSECUTION (10 pages)
- 5. 01-23-2009 NPL NPL Documents PROSECUTION (26 pages)
- 6. 01-23-2009 NPL NPL Documents PROSECUTION (7 pages)
- 7. 01-23-2009 NPL NPL Documents PROSECUTION (2 pages)
- 8. 01-23-2009 NPL NPL Documents PROSECUTION (13 pages)
- 9. 01-23-2009 NPL NPL Documents PROSECUTION (6 pages)
- 10. 01-23-2009 NPL NPL Documents PROSECUTION (4 pages)
- 11. 01-23-2009 NPL NPL Documents PROSECUTION (4 pages)
- 12. 01-23-2009 NPL NPL Documents PROSECUTION (2 pages)
- 13. 01-23-2009 NPL NPL Documents PROSECUTION (12 pages)
- 14. 01-23-2009 NPL NPL Documents PROSECUTION (7 pages)
- 15. 01-23-2009 FOR Foreign Reference PROSECUTION (48 pages)
- 16. 01-23-2009 FOR Foreign Reference PROSECUTION (46 pages)

Item 1. listed above contains the "Claims filed December 15, 2008 in Application No. 10/486,639" listed on the PTO 1449 Form filed January 23, 2009.

Item 2, listed above contains the following documents listed on the PTO 1449 Form filed January 23, 2009:

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"Claims filed December 15, 2008 in Application No. 10/486,639";

Pitt et al. "Glutamate Excitotoxicity in a Model of Multiple Sclerosis". Nature. 2000; 6(1):67-70;

Bever et al. The effects of 4-aminopyridine in multiple sclerosis patients: Results of a randomized, double-blind, placebocontrolled, crossover-trial. Neurology, 1994 Vol. 44:1054-1059;

Bever et al. Treatment with oral 3,4 diaminopyridine improves leg strength in multiple sclerosis patients: Results of a randomized, double-blind, placebo-controlled, crossover-trial. Neurology, 1996 Vol. 47:1457-1462;

Rasdn et al. Cloning and characterization of a CAMP-specific phosphodiesterase (TbPDE2B) from Trypanosoma brucei. PNAS, 2002 Vol. 99:4714-4719;

Ward et al., "Pentoxifylline-A Review of its Pharmacodynamic and Pharmacokinetic Properties, and its Therapeutic Efficacy", Drug Evaluation, Drugs 34: 50-97 (1987);

Leigh et al., "Excitotoxicity in ALS", Nerol. 1996 47 (Supp 4), S221-7;

Ludolph et al., "The role of excitotoxicity in ALS - what is the evidence?", J. of Neurol. 2000, 247 (Supp 1) 7-16;

Rothstein, "Excitotoxicity and Neurodegeneration in Amyotrophic Lateral Sclerosis", Clin Neurosc 95-96 3(6) 348-59;

Rothstein, "Excitotoxicity hypothesis", Neurol 1996 47 (Supp 4) S19-25;

Doble, "The pharmacology and mechanism of action of riluzole", AMERICAN ACADEMY OF NEUROLOGY, 1996, pp. S233-S241;

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Bar, "Motor neuron disease in vitro: the use of cultured motor neurons to study amyotrophic lateral sclerosis", EUROPEAN JOURNAL OF PHARMACOLOGY, 405, 2000, pp. 285-295;

Sommer et al, "Therapeutic potential of phosphodiesterase type 4inhibition in chronic autoimmune demyelinating disease", JOURNAL OF NEUROIMMUNOLOGY, 79, 1997, pp. 54-61;

Beghi et al, "A randomized controlled trial of recombinant interferon beta-1a in ALS", AMERICAN ACADEMY OF NEUROLOGY, 2000, pp. 469-473;

Jahn et al, "Mechanism of block of nicotinic acetylcholine receptor channels by purified IgG from seropositive patients with myasthenia gravis, AMERICAN ACADEMY OF NEUROLOGY, 2000, p. 474;

Asahara et al, "Glutamate enhances phosphorylation of neurofilaments in cerebellar granule cell culture", JOURNAL OF THE NEUROLOGICAL SCIENCES, 171, 1999, 84-87 (first page attached);

Houslay, PROGRESS IN NUCLEIN ACID RESEARCH AND MOLECULAR BIOLOGY, Vol. 69, 1001, 249-315 (first page attached);

Snider et al, "Signaling the Pathway to Regeneration", NEURON 2002, 35, 13-6 (first page attached);

Santos et al, "Cyclic AMP increases the survival of ganglion cells in mixed retinal cell cultures in the absence of exogenous neurotrophic molecules, an effect that involves cholinergic activity", BRAZ J. MED BIOL RES, 2001m, 34, 1585-1593, pp. 1585-1593 (first page attached);

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Feldman et al, "Breathing: Rhythmicity, Plasticity, Chemosensitivity", ANNU REV NEUROSCI 2003, 26, pp. 239-266 (first page attached);

Polman et al, "Clinical review: Drug treatment of multiple sclerosis", BMJ, Volume 321, 19-26 August 2000, pp. 490-494; and

Compston et al, "Multiple sclerosis", THE LANCET, Vol. 359, April 6, 2002, pp. 1221-31.

Item 3, listed above contains the following document listed on the PTO 1449
Form filed January 23, 2009:

Branch, "A good antisense molecule is hard to find", TIBS, 23, February 1998, pp. 45-50.

Item 4, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Cherry et al, "Diazepam and rolipram differentially inhibit cyclic AMP-specific phosphodiesterases PDE4A1 and PDE4BE in the mouse", BIOCHEMICA ET BIOPHYSICA ACTA 1518, 2001 PP. 27-35.

Item 5, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Crooke, "Basic Principles of Antisense Therapeutics", Chapter 1, pp. 1-50.

Item 6, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Dinter, "Phosphodiesterase Type 4 Inhibitors", BioDrugs, Feb. 2000, 13 (2), pp. 87-94.

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Item 7, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Friedman et al, "A Pilot Study of Pentoxifylline in Multiple Schlerosis", ARCHIVES OF NEUROLOGY, October 1996, Vol. 53, pp. 956-957.

Item 8, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Jen et al, "Suppression of Gene Expression by Targeted Disruption of Messenger RNA: Available Options and Current Strategies", STEM CELLS 2000, 18:307-319.

Item 9, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Kempermann et al, "Functional significance of adult neurogenesis", Current Opinion in Neurobiology 2004, 14:186-191.

Item 10, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Mishra et al, "Calcium calmodulin and 3',5'-cyclic nucleotide phosphodiesterase activity in human muscular disorders", JOURNAL OF THE NEUROLOGICAL SCIENCES, 109, 1992, 215-218.

Item 11, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Myers et al, "Pentooxifylline is not a promising treatment for multiple sclerosis in progression phase", AMERICAN ACADEMY OF NEUROLOGY, 1998, pp. 1483-1486.

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Item 12, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Pihl-Carey, "Isis to Restructure as Crohn's Disease Drug Falls in Phase III",

BIOWORLD TODAY, vol. 10, 239, December 1999, pp. 1-2.

Item 13, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Price et al, "Mémoire: Amyotrophic lateral sclerosis and Alzheimer's disease.

Lessons from model systems", REV NEUROL (PARIS), 1997, 153: 8-9, pp. 484-495.

Item 14, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

van Oosten, "A pilot study investigating the effects of orally administered

pentoxifylline on selected immune variables in patients with multiple sclerosis",

JOURNAL OF NEUROIMMUNOLOGY, 1996, 66, pp. 49-55.

Item 15, listed above contains WO 00/40714, which is n listed on the PTO 1449

Form filed January 23, 2009.

Item 16, listed above contains WO 01/44449, which is n listed on the PTO 1449

Form filed January 23, 2009.

A copy of the following listed documents is not contained in the PTO IFW and

were not filed January 23, 2009: Brighina et al, "Recent Advances in the Therapy of

Amyotrophic Lateral Sclerosis: Focus on Excitotoxicity", FUNCTIONAL NEUROLOGY

(16), Suppl. 4, 2001, pp. 189-292; and Rowland et al, "Amyotrophic Lateral Sclerosis",

N. ENGL. J. MED., Vol. 344, No. 22, May 31, 2001, pp. 1688-1700. The undersigned

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has requested a copy of these documents and will file same once received by the undersigned.

The following is a copy of the undersigned's receipts from the January 23, 2009 filing of the listed documents.

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Electronic A	cknowledgement Receipt			
EFS ID:	4666446			
Application Number:	10560774			
International Application Number:				
Confirmation Number:	5165			
Title of Invention:	Use of pyrazolopyridines for the treatment of cognitive deficits			
First Named Inventor/Applicant Name:	Fablen Schweighoffer			
Customer Number:	23117			
Filer:	B. J. Sadoff/Pachack Phoremachanh			
Filer Authorized By:	B. J. 5sdoff			
Attorney Docket Number:	815-9665-167			
Receipt Date:	23-JAN-2009			
Filing Date:	14-DEC-2008			
Time Stamp:	15:25:38			
Application Type:	U.S. National Stage under 33 USC 371			

## Payment information:

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JANUARY 23, 2009

Return of an initialed copy of the PTO 1449 Forms filed January 23, 2009, as acknowledgement of consideration of the filed documents, pursuant to MPEP § 609, is requested.

The present Request is not being filed in response to the Office Action of April 20, 2009.

Respectfully submitted,

## **NIXON & VANDERHYE P.C.**

By: /B. J. Sadoff/
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